82

Ultra

09/549463

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=> fil medl,hcaplus,biosis,embase,jicst,wpids
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                               0.21       0.21

FILE 'MEDLINE' ENTERED AT 15:44:56 ON 03 JUN 2002

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=> s (adenovir? e1a or e1a or e1a protein or antigen?(a)viral(a)(tumor or tumour)
or oncogene?(a)protein?(a)viral or transcript? factor? or adenovir? early protein?)
L1        71389 FILE MEDLINE
L2        78951 FILE HCAPLUS
L3        49061 FILE BIOSIS
L4        44344 FILE EMBASE
L5         7321 FILE JICST-EPLUS
L6         1209 FILE WPIDS

TOTAL FOR ALL FILES
L7       252275 (ADENOVIR? E1A OR E1A OR E1A PROTEIN OR ANTIGEN?(A) VIRAL(A)(TUM
                OR OR TUMOUR) OR ONCOGENE?(A) PROTEIN?(A) VIRAL OR TRANSCRIPT?
                FACTOR? OR ADENOVIR? EARLY PROTEIN?)

=> s e1b or e2a
L8         1363 FILE MEDLINE
L9         1728 FILE HCAPLUS
L10        1396 FILE BIOSIS
L11        1156 FILE EMBASE
L12          56 FILE JICST-EPLUS
L13         177 FILE WPIDS

TOTAL FOR ALL FILES
L14        5876 E1B OR E2A

=> s (17 or 114) and (eukaryo? or mammal? or human)(a)cell!
L15        2055 FILE MEDLINE
L16        2420 FILE HCAPLUS
L17        1375 FILE BIOSIS
L18        1237 FILE EMBASE
L19          43 FILE JICST-EPLUS
L20         131 FILE WPIDS

TOTAL FOR ALL FILES
L21        7261 (L7 OR L14) AND (EUKARYO? OR MAMMAL? OR HUMAN)(A) CELL!

=> s l21 and (erythropoietin? or glycoprotein hormone? or
receptor?(a)erythropoietin? or anemia disease or erythropoiesis)
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Searched by: Mary Hale 308-4258 CM-1 12D16

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L22          15 FILE MEDLINE
L23          35 FILE HCAPLUS
L24          11 FILE BIOSIS
L25          14 FILE EMBASE
L26           0 FILE JICST-EPLUS
L27           4 FILE WPIDS

TOTAL FOR ALL FILES
L28          79 L21 AND (ERYTHROPOIETIN? OR GLYCOPROTEIN HORMONE? OR RECEPTOR?(A
                ) ERYTHROPOIETIN? OR ANEMIA DISEASE OR ERYTHROPOIESIS)

=> s l28 and ((post or peri)(a)(modif? or transl?) or posttransl? or peritransl?)
L29           0 FILE MEDLINE
L30           1 FILE HCAPLUS
L31           0 FILE BIOSIS
L32           0 FILE EMBASE
L33           0 FILE JICST-EPLUS
L34           1 FILE WPIDS

TOTAL FOR ALL FILES
L35           2 L28 AND ((POST OR PERI)(A)(MODIF? OR TRANSL?) OR POSTTRANSL? OR
                PERITRANSL?)

=> dup rem l35
PROCESSING COMPLETED FOR L35
L36           2 DUP REM L35 (0 DUPLICATES REMOVED)

=> d cbib abs 1-2

L36  ANSWER 1 OF 2  WPIDS (C) 2002 THOMSON DERWENT
AN   2000-665247 [64]   WPIDS
AB   WO 200063403 A UPAB: 20001209
     NOVELTY - A method (M1) of producing recombinant proteins in a eukaryotic
     cell, preferably a human cell line, which comprises a sequence encoding at
     least one E1 protein of an adenovirus or its functional homologue,
     fragment or derivative, is new. The cell does not encode a structural
     adenoviral protein from its genome or from a sequence integrated into the
     genome.
          DETAILED DESCRIPTION - A method (M2) of producing recombinant
     proteins in a eukaryotic cell, preferably a human cell line, which
     comprises a sequence encoding at least one E1 protein of an adenovirus or
     its functional homologue, fragment or derivative, is new. The cell does
     not encode a structural adenoviral protein from its genome or from a
     sequence integrated into the genome.
          The method comprises providing the cell with a gene encoding a
     recombinant protein, culturing the cell in a suitable medium and
     harvesting the protein substance from the cell and/or medium.
          INDEPENDENT CLAIMS are also included for the following:
          (1) a method (M2) for enhancing production of a recombinant protein
     in a eukaryotic cell, comprising providing a eukaryotic cell with a
     nucleic acid encoding at least part of the protein, where the coding
     sequence is under control of a Cytomegalovirus (CMV) promoter, an
     E1A promoter, or their functional homologues, derivatives and/or
     fragments and further providing the cell with an E1A activity or
     E1A-like activity;
          (2) a recombinant mammalian cell immortalized by the presence of at
     least one adenoviral E1 protein or its functional derivative, homologue
     and/or fragment, and further comprising a nucleic acid (N1) in a
     functional format for expressing at least one variable domain of an
     immunoglobulin or its functional derivative, homologue and/or fragment;
          (3) a method (M3) for producing at least one variable domain of an
     immunoglobulin, comprising culturing the recombinant mammalian cell of
```

(2);

(4) an immunoglobulin or its functional part, homologue and/or derivative, obtainable by the method of (M3);

(5) a recombinant protein obtained by the method of M1, M2 or M3, where the recombinant protein has a human glycosylation pattern different from the isolated natural counterpart protein;

(6) a recombinant **erythropoietin** molecule obtained by the method of M1 or M2;

(7) a human cell having a genomic sequence encoding at least one E1 protein of an adenovirus or its functional derivative, homologue or fragment, where the cell does not produce structural adenoviral proteins and has a gene encoding a recombinant protein; and

(8) a viral protein obtained by the method of M1 or M2, where the viral protein is free from any non-human mammalian proteinaceous material.

ACTIVITY - None given.

No biological data given.

MECHANISM OF ACTION - Vaccine.

No biological data given.

USE - The recombinant **mammalian cells** are useful for producing variable domains of an immunoglobulin which have **post-translational** modifications different than that of their isolated natural counterparts. The **human cells** having a genomic sequence encoding at least one E1 protein of an adenovirus or its functional derivative, homologue or fragment are useful for the production of a recombinant protein, e.g. a viral protein for use in a vaccine. The adenoviral **E1B** protein or its functional derivative, homologue and/or fragment has anti-apoptotic activity and is useful for enhancing the production of a proteinaceous substance in a eukaryotic cell (all claimed).

ADVANTAGE - The cell is capable of producing 2 to 200 fold more recombinant protein and/or proteinaceous substances than conventional mammalian lines such as Chinese Hamster Ovary (CHO), COS cells, vero, Hela, BHK or Sp-2 cell lines. Specifically, the human cell is capable of producing in excess of 100, preferably 5000, units **erythropoietin** /million cells in 24 hours (claimed).

Dwg.0/24

L36 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2002 ACS

1999:457101 Document No. 132:47942 Regulation of cellular 15-lipoxygenase activity on pretranslational, translational, and **posttranslational** levels. Kuhn, Hartmut; Heydeck, Dagmar; Brinckman, Roland; Trebus, Frank (Institute of Biochemistry, University Clinics Charite, Humboldt University, Berlin, D-10115, Germany). Lipids, 34(Suppl., Fatty Acids and Lipids from Cell Biology to Human Diseases), S273-S279 (English) 1999. CODEN: LPDSAP. ISSN: 0024-4201. Publisher: AOCS Press.

AB A review with 34 refs. with an emphasis on the author's results. In **mammalian cells**, enzymic lipid peroxidn. catalyzed by 12/15-lipoxygenases is regulated by pretranslational, translational, and **posttranslational** processes. In rabbits, rats, and mice induction of exptl. anemia leads to a systemic up-regulation of 12/15-lipoxygenases expression. In addn., interleukins-4 and -13 were identified as strong up-regulators of this enzyme in human and murine monocyte/macrophages and in the lung carcinoma cell line A549, and the interleukin-4(13) cell surface receptor as well as the signal transducer and activator of transcription 6 (STAT6) appears to be involved in the signal transduction cascade. On the level of translation, 15-lipoxygenase synthesis is blocked by the binding of regulatory proteins to a characteristic guanine-cytosine-rich repetitive element in the 3'-untranslated region of the rabbit 15-lipoxygenase mRNA, and the formation of such 15-lipoxygenase mRNA/protein complexes was identified as mol. reason for the translational inactivity of the 15-lipoxygenase mRNA in immature red blood cells. However, proteolytic breakdown of the regulatory proteins which were

recently identified as hnRNP K and hnRNP E1 overcomes translational inhibition during later stages of reticulocyte maturation. For maximal intracellular activity, 12/15-lipoxygenases require a rise in cytosolic calcium concn. inducing a translocation of the enzyme from the cytosol to cellular membranes as well as small amts. of preformed hydroperoxides which act as essential activators of the enzymes. 12/15-Lipoxygenases undergo irreversible suicide inactivation during fatty acid oxygenation, and this process may be considered an element of down-regulation of enzyme activity. Suicide inactivation and proteolytic breakdown may contribute to the disappearance of functional 12/15-lipoxygenase at later stages of **erythropoiesis**.

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	27.16	27.37

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.62	-0.62

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